REMARKS

Reconsideration is requested.

The specification has been amended to include the cross-reference to the PCT application and the relation of the present application of the same, in response to the Examiner's comments on page 2 of the Office Action dated July 13, 2004.

With regard to the restriction requirement in the Examiner's comments on page 2 of the Office Action dated July 13, 2004, reconsideration is requested at least insofar as the grouping of claims 26 and 49-52 with the elected group which the Examiner has characterized as being "drawn to DNA vaccine". See, page 2 of the Office Action dated October 2, 2003. The applicants note that claims 26 and 51 are depended on claims 18 and 15, respectively, which are each included in the Examiner's Group V and the Examiner is requested to reconsider whether claims 26 and 51 would more appropriately be grouped with the subject matter of the Examiner's Group V. Moreover, claims 49 and 50 both depend from claim 19 which the Examiner has included in the subject matter of the Examiner's Group VI and regrouping of claims 49 and 50 with the subject matter of Group VI may be more appropriate. Finally, claim 52 is depended on claim 35 which is included in the Examiner's Group VIII and the Examiner is requested to reconsider whether the subject matter of claim 52 should more appropriately be included with the subject matter of the Examiner's Group VIII.

The specification has been amended above to include sequence identifiers as well as the attached new Sequence Listing. The attached paper and computer-readable copies of the Sequence Listing are submitted to be the same. No new matter has been added.

The objection to claims 26 and 49-52 stated on page 3 of the Office Action dated July 13, 2004, are noted and the Examiner is requested to see the above comments with regard to the restriction requirement in response.

The Section 112, second paragraph, rejection of claims 4-8, 26 and 49-52 stated on page 4 of the Office Action dated July 13, 2004, are believed to be obviated with regard to claims 4-8 in view of the above amendments. Clarification is requested however with regard to claims 26 and 49-52 in the event the restriction requirement is maintained as originally-grouped. Withdrawal of the Section 112, second paragraph, rejection is requested.

The Section 103 rejection of claims 4-8, 26 and 49-52 over Fomsgaard (Immunology Letters 1999, Vol. 65, pp 127-131), Schreiber (1997, Journal of Virology, Vol. 71, pp 9198-9205) and Tartar (U.S. Patent No. 2,677,363), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The applicants submit that none of the documents cited by the Examiner, neither alone nor in combination, renders obvious the subject matter of the present claims. More particularly, the disclosure of Formsgaard is limited to a general statement according to which DNA-based vaccines are suggested, at best, to offer certain advantages over classical vaccines in the prophylaxis against HIV-1. Similarly, the publication of Schreiber merely describes that the V3 loop of HIV gp120 contains hypervariable regions which contain neutralizing epitopes.

The Examiner is understood to conclude that from the background of the cited prior art, it would have been obvious for the ordinarily skilled person to use random

and/or degenerate nucleotides on multiple plasmids to create sequences of the hypervariable region. In this context, the Examiner is understood to outline that the person of ordinary skill in the art would have known the different sequences of the V3 loop found in different isolates, e.g. from the disclosure of Tartar. The applicants respectfully submit that the claimed invention would not have been obvious over the cited art.

On the one hand, the present invention is particularly superior over the cited prior art, as it provides a method for generating a tremendously large number of different sequence variants. In fact, mixtures of **up to 10^5 to 10^6 or more** different sequence variants can be generated. The applicants believe that it was not possible to prepare such mixtures by employing the methods known in the cited art in a predictable or economic manner.

Moreover, the presently claimed invention advantageously provides for DNA vaccines comprising **randomly distributed** sequence variants. Within these vaccines, each sequence variant occurs statistically with the same frequency. In comparison, the sequence variants of the V3 loop observed in clinical samples are often the result of a selection process in the respective patient so that the occurrence of certain variants is increased. Here, it is particularly important for the Examiner to appreciate that, due to the random distribution of the sequence variants therein, the vaccines of the presently claimed invention contain a plurality of variants which have not (yet) been identified in any sample derived from a patient. However, it is possible that such virus variants could evolve in the near future. This means, an immunologic response against a putative virus variant can be induced and activated even before that variant has been observed in a

patient (see page 8 of the application text, last sentence of the first paragraph). None of the vaccines prepared according to the methods described in the cited prior art, or combination of art, are capable of preparing the advantageous vaccines of the presently claimed invention, since these vaccines are exclusively based on virus variants which already have been observed in infected patients.

The presently claimed invention provides for promising possibilities for the therapeutic and prophylactic treatment of HIV which could not have been foreseen from the cited prior art.

Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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